Department of Health and Human Services

PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF MENTAL HEALTH

National Advisory Mental Health Council

Minutes of the 200th Meeting

May 10, 2002

Minutes of the 200th Meeting
of the National Advisory Mental Health Council

The National Advisory Mental Health Council (NAMHC) convened its 200th meeting in closed session for the purpose of reviewing grant applications at 10:30 a.m. on May 9, 2002, at the Neuroscience Center in Rockville, Maryland, and adjourned at approximately 5:30 p.m. (see Appendix A: Review of Applications). The NAMHC reconvened in open session at 8:40 a.m. on May 10, 2002, in Conference Room 6C6, Building 31, at the main campus of the National Institutes of Health (NIH) in Bethesda, Maryland. In accordance with Public Law 92-463, this policy meeting was open to the public until its adjournment at 12:30 p.m. Richard K. Nakamura, Ph.D., Acting Director, National Institute of Mental Health (NIMH), chaired the meeting.

Council Members Present at Closed and/or Open Sessions (see Appendix B for Council Roster):

Mary L. Durham, Ph.D.
Javier I. Escobar, M.D.
Susan Folkman, Ph.D.
Megan R. Gunnar, Ph.D.
Norwood W. Knight-Richardson, M.D.
Jeffrey A. Lieberman, M.D.
James L. McClelland, Ph.D.
James P. McNulty
Charles B. Nemeroff, M.D., Ph.D.
Eric J. Nestler, M.D., Ph.D.
Edward Scolnick, M.D.
Larry R. Squire, Ph.D.
Ming T. Tsuang, M.D., Ph.D.
Roy C. Wilson, M.D.

Chairperson
Richard K. Nakamura, Ph.D.

Executive Secretary
Jane A. Steinberg, Ph.D.

Ex-Officio Council Members and Liaison Representative Present at Closed and/or Open Sessions:
Michael J. English, J.D.
Robert Freedman, M.D.
E. Cameron Ritchie, M.D.

Guest Speaker at Open Policy Session:
Greg Koski, Ph.D., M.D., Office of Human Research Protections (OHRP), DHHS

Others Present at Open Policy Session:
Rupert Ambrose, MesiMax Resources, Inc.
Lizbet Boroughs, American Psychiatric Association
Nancy Bateman, National Association of Social Workers
Scott Brawley, AIDS Action
Jill Egeth, Federation of Behavioral, Psychological and Cognitive Sciences
Diane Feirman, American Group Psychotherapy Association

Sarah Gehlert, The University of Chicago
Rebecca Goodman, Society for Research in Child Development
Lee Herring, American Sociological Association
Beth Kaplanek, Children and Adults with Attention-Deficit/Hyperactivity Disorder
Gary Kennedy, American Association for Geriatric Psychiatry
Andrew Kessler, American Psychological Society
Marjorie Kitzes, Child & Adolescent Bipolar Foundation
Leticia Lantican, University of Texas at El Paso
Monica Latham, American Public Health Association
Steven Mirin, American Psychiatric Association
Merrill M. Mitler, Sleep Research Society
Leonard Mitnick, Former NIMH staff member
Pamela S. Moore, Capitol Publications
Natalie Ochs, The Blue Sheet
Amy Parsley, American Association of Children's Residential Treatment Centers
Colleen Quinn, Child and Adolescent Bipolar Foundation
Gordon Raley, National Mental Health Association
Stephanie Reed, American Association for Geriatric Psychiatry
Darrel Reiger, American Psychiatric Association
Kurt Salsinger, American Psychological Association
Mary Jean Schumann, American Nurses Association
Paul Seifert, International Association of Psychosocial Rehabilitation Services
Deborah Shelton, International Society for Psychiatric-Mental Health Nurses ISPN
Andy Shih, National Alliance for Autism Research
Judy Stange, Access Consulting International
Karen Studwell, American Psychological Association
Allison Wainick, Society for Neuroscience
Patricia Watson, National Center for Post-Traumatic Stress Disorder
Sheldon R. Weinberg, CDM Group, Inc.
Jerry Weyrauch, Suicide Prevention Advocacy Network USA, Inc.
Joan Zlotnik, Institute for the Advancement of Social Work Research

OPEN POLICY SESSION: CALL TO ORDER

Dr. Richard K. Nakamura, Acting Director, NIMH, and Chairman, NAMHC, convened the Open Policy Session of the 200th Council meeting at 8:40 a.m. on May 10, 2002, in Building 31, Conference Room 6C6, on the campus of NIH in Bethesda, Maryland. After welcoming those present, Dr. Nakamura took note of the historic 200th meeting of the NAMHC.

CELEBRATING COUNCIL'S 200TH MEETING

Dr. Nakamura highlighted NIMH's growth and Council's role in the many changes that have taken place over the years. On July 3, 1946, President Truman signed the National Mental Health Act, which called for the establishment of a National Institute of Mental Health. The first meeting of the National Advisory Mental Health Council was convened on August 15, 1946, and shortly thereafter, the Public Health Service Division of Mental Hygiene awarded the first mental health research grant, entitled "Basic Nature of the Learning Process," to Dr. Winthrop N. Kellogg of Indiana University. On April 15, 1949, NIMH—one of the first six NIH institutes—was formally established. Dr. Robert H. Felix served as the first NIMH Director.

The ensuing 50 years of research introduced many new frontiers. Dr. Seymour Kety, the first Scientific Director at NIMH, established a strong mental health research base that was key to developing a brain neuroscience research capability on the NIH campus. Many scientists credit Dr. Kety's work as influential in advancing research not only in mental health but also in neuroscience and substance abuse.

Other milestones in the rapid expansion of NIMH's research activities included the Mental Health Study Act of 1955 signed by President Dwight D. Eisenhower and the Mental Retardation Facilities and Community Mental Health Construction (CMHC) Act of 1963 signed by President John F. Kennedy. During the mid-1960s, President Lyndon B. Johnson pledged his support to apply scientific research to social problems. Also during this time, amendments to the CMHC Act authorized grants to help pay the salaries of professional and technical personnel in federally funded Community Mental Health Centers. Meanwhile, Dr. Stanley F. Yolles advanced from his original position as Deputy Director to become the second NIMH Director in 1964. In 1966, NIMH had become the largest single institute within NIH and held 26 percent of its overall budget. In 1967, NIMH was separated from NIH and raised to bureau status until 1968 when it became a component of the Health Services and Mental Health Administration, only eventually to become a part of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), authorized by President Richard M. Nixon. In 1970, Dr. Julius Axelrod, an NIMH researcher, won the Nobel Prize in Physiology or Medicine for research into the chemistry of nerve transmission resulting in "discoveries concerning the humoral transmitters in the nerve terminals and the mechanisms for their storage, release and inactivation."

Dr. Bertram S. Brown was appointed as the third NIMH Director in 1970 and served in that capacity until 1977. The fourth NIMH Director, Dr. Herbert Pardes, who was appointed in 1978, continued to emphasize the importance of mental health services while simultaneously strengthening the Institute's research focus. NIMH played a critical role in developing brain-imaging technologies such as positron emission tomography (PET) that could produce visual representations of the functioning brain. In the late 1970s, President Carter's wife, First Lady Rosalynn Carter, became a vocal advocate for improving the nation's mental health and brought favorable attention to the field and to NIMH. Meanwhile, Dr. Roger Sperry became NIMH's second Nobel Laureate in 1981.

The election in 1980 of Ronald Reagan as the 40th president of the United States heralded significant changes for NIMH. Among the most notable was the introduction of Federal block grants to the states for mental health and other health services, which relieved NIMH of responsibility for categorical support of community mental health service programs. In 1984, Shervert H. Frazier, M.D., was appointed Director; among the hallmarks of his tenure was development of the NIMH National Plan for Schizophrenia Research. In 1987, administrative control of St. Elizabeths Hospital in the District of Columbia was transferred from NIMH to the District government.

Dr. Lewis L. Judd, who became the sixth NIMH Director in 1988, instituted a series of public hearings around the country that helped develop a nationwide constituency. He also presided over a period of unprecedented growth for NIMH, leading to the Decade of the Brain during President George H. W. Bush's administration, when the Institute became even more committed to neuroscience. During Dr. Frederick K. Goodwin's directorship of NIMH from 1992 to 1994, the Institute rejoined NIH.

In 1996, during the presidency of William J. Clinton, Dr. Steven E. Hyman became the eighth and most recent NIMH Director. His accomplishments included involving the people who need services in defining the Institute's research agenda. For example, he set up meetings with groups around the country, including local populations in Alaska, Texas, Pennsylvania, and youth advocates in Illinois. Among his other achievements were initiating careful evaluation of research gaps and opportunities, resulting in Council reports on bridging science and services, genetics, child and adolescent research, and translating behavioral science into action.

Council workgroups also drafted numerous special reports to help guide the Institute's actions. Of particular importance was Council's role in examining parity in mental health reimbursement. Also notable was the Intramural Research Program Planning Committee's report *Finding the Balance* that reinvigorated the intramural program. The interest of former Surgeon General Dr. David Satcher in mental health was undergirded by Council members' support of his development of a national plan for suicide prevention as well as the first-ever, landmark Surgeon General's Report on Mental Health, and supplemental reports on youth violence and on mental health in the context of race, culture, and ethnicity.

NIMH's commitment to basic science was recognized again in 2000 when long-term grantees of NIMH, Drs. Paul Greengard and Eric Kandel, shared the Nobel Prize in Physiology or Medicine with Dr. Arvid Carlsson.

Concluding this celebratory presentation, Dr. Nakamura noted that the number of NIMH staff now exceeds that of the original NIH. Much of the credit for NIMH's growth and its reputation as a national leader in neuroscience must go to an advisory council that, through written reports and strong vocal opinions, keeps the Institute committed to good science and to those persons with mental illness.

NIMH ACTING DIRECTOR'S REPORT

Dr. Nakamura began by recounting President Bush's pledge of support in April for obtaining parity for mental health insurance coverage. While cautious about potential increases in insurance costs, the President said that Americans with mental disorders deserve a healthcare system that treats their illnesses with the same urgency that it treats physical illnesses and that he would work with congressional leaders from both parties to pass parity legislation this year (see http://www.whitehouse.gov/news/releases/2002/04/20020429-1.html).

At the same time, President Bush announced the establishment of a New Freedom Commission on Mental Health, which will have a maximum of 15 appointed members, including providers, payers, administrators, and consumers of mental health services and their family members. The Commission will also have a maximum of seven ex-officio members from Federal Government agencies. Dr. Michael Hogan, a former member of this Council and Director of the Ohio Department of Mental Health, will chair the group. As indicated in a Presidential Executive Order, within a year this Commission is expected to conduct a comprehensive study of the U.S. mental health service delivery system and to recommend improvements that enable persons with serious mental illness to "live, work, learn, and participate fully in their communities" (see http://www.mentalhealthcommission.gov).

On March 26, the President nominated Dr. Elias Zerhouni as NIH Director and Dr. Richard Carmona as Surgeon General. Congress confirmed Dr. Zerhouni, then Executive Vice Dean and Professor of Radiology and Biomedical Engineering at the Johns Hopkins School of Medicine, on May 2. Dr. Nakamura said that NIH welcomes the appointment of this very talented, positive, and broad-thinking scientist who is also reputed to be an excellent administrator.

Meanwhile, the search for a new NIMH Director continues; a number of highly qualified candidates have expressed interest through a wide-open search.

Requests are already being processed under the new congressionally approved program that encourages patient-oriented researchers to enter the field of mental health research by promising Federal loan repayment subsidies for up to $35,000 per year. While this amount may not be a sufficient enticement for applicants who have debts approaching $500,000, it is likely to make a big difference in decisions by clinicians regarding whether they can plan a research career as opposed to going directly into a practice setting.

Dr. Nakamura also reported a number of staff changes. Ms. Gemma Weiblinger, Special Assistant to the Director, NIMH, and the Acting Director for the Office of Science Policy and Program Planning (OSPPP), was appointed Director of the newly established Office of Constituency Relations and Intergovernmental Activities (OCRIA). She will oversee the Institute's public liaison and outreach activities, manage interactions with numerous constituency groups, and be the principal contact within the Institute for state and local governments as well as other sections of the Federal Government. In turn, Dr. Wayne Fenton, NIMH Acting Deputy Director, also will assume responsibilities as Acting Director of OSPPP.

Other staffing changes include the designation of Dr. Eve Moscicki as the NIMH Acting Associate Director for Child and Adolescent Research. She will chair the NIMH Child Research Consortium. Dr. Benjamin Xu joined the Extramural Review Branch within the Division of Extramural Activities (DEA). In the Division of Mental Disorders, Behavioral Research and AIDS (DMDBA), Dr. Timothy Cuerdon was hired as Chief of the Adherence and Behavioral Change Research Program in the Health and Behavioral Science Research Branch. Dr. Kathy Kopnisky joined the Center for Mental Health Research on AIDS (CMHRA). Finally, Dr. Euthymia Hibbs retired in April as Chief of the Psychosocial Treatments Research Program in the Child and Adolescent Treatment and Preventive Intervention Research Branch, Division of Services and Intervention Research (DSIR).

Approval of the Minutes/Schedule of Future Council Meetings

Dr. Nakamura requested and received a motion to approve the minutes of the January 25, 2002, NAMHC meeting, which was seconded and passed unanimously without further discussion. Dr. Jane Steinberg, Executive Secretary, called attention to the scheduled dates for future Council meetings.

PROTECTING HUMAN RESEARCH SUBJECTS

Dr. Nakamura introduced the first speaker, Dr. Greg Koski, who directs the new Office of Human Research Protections (OHRP) in the Department of Health and Human Services (DHHS). Dr. Koski also chairs the Human Subjects Research Subcommittee of the National Science and Technology Council's Committee on Science.

In outlining his presentation, Dr. Koski said he wanted to describe what OHRP is trying to accomplish and one of the critical issues it is addressing—the conduct of research involving subjects with impaired decision-making capabilities, including children. He began by stressing that OHRP was established not only to strengthen the system for protecting human subjects but also to improve the whole approach to conducting human research—because the two are inseparable. Plans for OHRP involve collaborations with the NIH, the Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC), as well as other Federal agencies.

Dr. Koski said that OHRP is emphasizing a collaborative and programmatic approach that encourages more direct communications and partnerships among all key research participants (patients, volunteers, researchers, sponsoring organizations, regulators, and funders) to achieve common goals, especially the effective protection of research subjects. He indicated that OHRP also is striving to improve overall coordination as a way of shifting some burdens away from Institutional Review Boards (IRBs).

For the past 18 months, OHRP has been laying the groundwork for a more proactive operational mode. This has entailed redesigning the assurance process under which grants are awarded and establishing the regulatory authority for OHRP. By simplifying formerly cumbersome processes, resources that were largely allocated to paperwork are being diverted to more direct

efforts to improve human subject protections. Concomitantly with the infrastructure changes, OHRP has been building new programs, dramatically expanding educational activities, and holding teleconferences, town meetings, and other types of training events for investigators and IRB members. This effort will be extended in the year ahead to public education, since it is critical that laypersons be well informed about the issues entailed in safeguarding human research subjects and the meaning of informed consent. This is particularly crucial now that bioterrorism poses new challenges to research involving humans.

The single most important change in the shift to a proactive paradigm is the switch to a prevention-focused quality improvement program in which staff from the OHRP, in collaboration with other colleagues throughout DHHS, help research institutions assess the strengths and weaknesses of their own programs. Any identified weaknesses will be used as opportunities for system improvements. Accountability is an essential feature of these changes. As noted in the Inspector General's report, too much reliance has been placed on simple trust—without scrutiny or verification. An effective quality improvement program must be coupled with expanded surveillance and oversight, and the relationship between overseers and those they regulate must entail a more collaborative interaction with less confrontation than previously exerted.

The human protections system also must be assessed. Hence, DHHS, with generous support from NIH, has asked the Institute of Medicine (IOM) to recommend objective effectiveness measures for evaluating programs for the protection of human subjects. Approaches or procedures that do not appear to be contributing effectively to protections but rather pose impediments to research will be eliminated.

Turning to a different topic, Dr. Koski reported the establishment of a National Human Research Protections Advisory Committee (NHRPAC) as a forum for broad-based discussions of ethical issues and related policies pertaining to the conduct of human research. This body has been considering two vital issues: the nature of additional protections that might be afforded adults with impaired decision-making abilities and whether changes are needed in the protections provided for minors under sub-part D of the Health and Human Services (HHS) regulations for children (see http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm).

The first issue, which has been under discussion for some time, previously has focused primarily on persons with mental diseases—many of whom were institutionalized. The National Bioethics Advisory Commission (NBAC), which is no longer active, took up the issue and published a report (see http://www.georgetown.edu/research/nrcbl/nbac/capacity/TOC.htm). That report, *Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity*, contains 21 recommendations that "…would both enhance existing protections and facilitate broad public support for continued research on mental disorders" (Executive Summary, page 3). When NIH convened a special workshop chaired by Dr. Ned Cassem to examine this topic, the mental health community reacted negatively to the implication that persons with a history of mental illness should be singled out for special restrictions. Furthermore, the group argued that the concept of diminished capacity should not focus primarily on those with mental illness.

Nonetheless, an Interagency Working Group established by DHHS to study the NBAC report concluded that most of the recommendations were solid and merited immediate endorsement. The OHRP has already started to implement specific recommendations such as notifying States' Attorney Generals about the need for greater clarity in state regulations regarding the definition of individuals who are legally authorized to give consent as opposed to those who lack consent capacity. This HHS Interagency Working Group also has addressed other issues such as the appropriate structure for review, approval, and oversight of research involving individuals with impaired decision-making capacity. The model recommended for adults with impaired decision-making capacity differed from that for children—notably, the category for research approval entailing "minor increase over minimal risk" that has been useful in some types of research involving children would be omitted. The workgroup requested additional information on that particular point as well as the appropriateness and applicability of a broader framework. More attention also was given to the issue of assessing independent capacity—how this should be accomplished, when, and by whom. Standards for this assessment process have not yet been set.

These issues and others have now been forwarded to the NHRPAC for its discussion and advice. After extensive deliberations, that body expects to make a final report to DHHS in the near future. Among expected recommendations are changes in the HHS regulations to provide greater protections for individuals with impaired decision-making abilities. The HHS Secretary must make any final determination, and new proposals must ultimately go through the appropriate process for public comment as well as the rule-making process if new regulations are involved.

Although extensive research involving children with various types of neurological and mental disorders is already underway, proposals to revise human subject protections for minors pose a dilemma. On the one hand, many of the medications in widespread use to treat children have never been adequately studied for safety and efficacy in that population; on the other hand, conducting the needed research to verify their appropriateness can expose children to further research risks. The NHRPAC is studying this issue, and Congress is expected to mandate a parallel study by the IOM. The general sense is that the regulations pertaining to children as research subjects are sound and sufficiently flexible for investigators to continue conducting well-designed studies. However, better guidance can be developed regarding what, for example, constitutes minimal risk and whether that is an absolute or a relative standard. Additionally, clearer definitions are needed, for example, regarding what constitutes a "minor increase over minimal risk" so that both investigators and IRBs can take consistent and appropriate actions.

In conclusion, Dr. Koski promised to provide Council members with an executive summary of the HHS Working Group's response to the NBAC report.

Discussion

Dr. Nakamura opened the discussion by asking what balance in human subject protections could ensure that persons with impaired capacity are better protected but not abandoned in research because the procedures become too onerous. Dr. Koski replied that various stakeholders have different perspectives on this issue, with a few taking the unfortunate stance that any research is

too risky. Although most of the public views research positively, general confidence in the human research process has diminished over the last few years. Serious work will be required to restore a widespread belief that research is worth conducting and that effective subject protections can be implemented. Additionally, more attention must be given to investigators' potential conflicts of either commitment or interest. Some of these challenges can be handled by using third-party advocates for individuals unable to make decisions for themselves. Under certain conditions, it may be appropriate to allow waivers of informed consent. Additionally, some models for emergency research may be applicable, but there are no easy answers to this ethical dilemma.

Dr. Ritchie, noting Dr. Koski's reference to bioterrorism, said that questions about psychological reactions to radiological, biological, or chemical terrorism—and how these might be mitigated—have become central issues at NIH and the Department of Defense. Unfortunately, little research in this field currently exists, and it has become very difficult in the wake of September 11 to obtain IRB approval of research protocols. Dr. Ritchie asked Dr. Koski if he had suggestions for informing IRBs in advance about the importance of research pertaining to disaster responses and developing an "off-the-shelf" protocol that could be used, if necessary.

Dr. Koski responded that Dr. Ritchie's concept of a human research preparedness plan made sense and should be advocated. In fact, he continued, OHRP and the NHRPAC's Workgroup on Human Subject Protections will be developing appropriate models that can be used in situations resembling the September 11 events. Following the destruction of the Twin Towers, a host of groups across the country descended upon New York City to study the psychosocial impact of the horrific event and were met with some resistance by clinicians who thought it potentially detrimental to impose on individuals whose lives were directly disrupted by the attacks or who were peripheral witnesses. This experience highlighted the need to make specific recommendations to IRBs regarding appropriate mechanisms, similar to those used for other emergency research, that could be implemented in advance for reviewing and approving research following bioterror disasters.

Dr. Fenton interjected that NIMH staff members Drs. Farris Tuma and Regina Dolan-Sewell are working with representatives of OHRP and the New York Academy of Sciences to design a workshop on those issues that will be held within the next 6 months. The agenda will focus on reviewing what is known about the potential risks and benefits to subjects participating in research following either a terrorist or bioterrorist attack, as well as developing guidelines for informing IRBs about what informed consent agreements are required in such situations. The underlying assumption is that any decision made about whether or not to participate in such research lies with the competent prospective research participant who has been given the best available evidence concerning potential benefits and risks.

Dr. Tsuang commented that based on his own experiences, there may be long delays in OHRP's response time to applicant institutions where study protocols may have been revised to address identified human subjects issues. Dr. Tsuang suggested that better communications and proactive interactions are badly needed and that these improvements may require additional manpower resources for OHRP. Additionally, he felt strongly that press releases about human

subject protection problems should not be issued by an oversight agency before the applicant institution has been informed about and has had an opportunity to respond to such concerns.

In response, Dr. Koski explained that he had recused himself from any questions or actions pertaining to Harvard University, its medical school, or any of its affiliates during the entire time of his government service. Dr. Koski noted, however, that specific policies govern the release of information by OHRP, which as a Federal regulatory agency is subject to procedures outlined in the Freedom of Information Act. He also acknowledged that there had been unacceptably long delays between the opening and closing of some of the compliance oversight cases. This was due, as Dr. Tsuang correctly observed, to the paucity of manpower within OHRP. When Dr. Koski was appointed to direct the Office, 184 complaint cases had already been opened with only two full-time staff to handle them. However, that backlog has been dramatically reduced to only 40 currently open cases.

The OHRP has, in total, managed more than 250 for-cause compliance oversight investigations and fully resolved about 171—with the remaining cases well on the way to closure. Of the 250 investigations, only 2 have required the kind of corrective actions taken at both the University of Oklahoma and Johns Hopkins University where larger systemic problems required detailed assessments of the entire human research protection programs. More than 99 percent of research institutions have taken steps over the last 2 years to strengthen human subject protection programs, addressing many of the deficiencies that existed nationwide. The situation promises to improve further as more proactive interactions with institutions are initiated.

In response to a question from Dr. Lieberman regarding the status of IRB certification, Dr. Koski explained that the term "certification" applies to individuals while the term "accreditation" pertains to programs, including human research protection programs. The DHHS has actively promoted voluntary, private-sector accreditation programs that complement the government's oversight role. This public-private partnership allows accredited institutions to demonstrate their commitment to exceed minimal regulatory requirements and fulfill a standard of excellence. The efforts of DHHS to catalyze this process by asking IOM to conduct a relevant study have stimulated the development of two private-sector accreditation programs that are now operational but not fully developed. The hope is that government-sponsored training programs will help prepare more institutions for accreditation. Sites that achieve accreditation are preferred both by research sponsors and by those who participate as research subjects because of the greater confidence that all work meets the highest standards.

Dr. Wilson questioned why the public is losing confidence in the protections afforded research subjects and what leadership the OHRP, the new Advisory Committee of the OHRP, and the broader research community can provide to reverse this negative opinion. In response, Dr. Koski commented that the public is often most fascinated by the events that the research community would least like to highlight, especially breakdowns in the system when someone is harmed or injured. Fortunately, the reservoir of public support for research has been very strong over the past 30 years, and public opinion has only wavered recently in the wake of serious problems. The public does need to be educated and to be given a balanced picture of what research actually involves as well as enlisted as a partner in the research process. The restoration of confidence in the system will take time but is critically important, not only for the public but also for investigators and for IRBs.

Dr. McClelland said that the new policies requiring investigators to certify their training in human subject protections issues raised questions for him regarding whether behavioral research should have subject protection procedures different from those for more general medical research. He noted that the training materials used by NIH focused primarily on infectious diseases and were difficult to translate into behavioral research settings.

Dr. Koski stressed that he is fully aware of—and a strong advocate for—the need to address issues surrounding protection of research subjects in social and behavioral science studies. OHRP has been working with the National Science Foundation as well as the American Psychological Association and the American Sociological Association (ASA) to develop guidance for the research community, particularly IRBs and investigators, about how regulations

for the protection of human subjects can be applied most effectively and efficiently. Dr. Koski noted that the NHRPAC has established working groups, including one for the social and behavioral sciences, co-chaired by Dr. Felice Levine from the ASA and Dr. Jeffrey Cohen of OHRP, that will be issuing some findings. The goal is to use those reports as guidance and educational materials. In a similar vein, the Public Responsibility in Medicine and Research Group was recently contracted to produce an interactive CD for investigators, although the group still focuses primarily on biomedical research. A similar educational tool for the social and behavioral sciences is needed, or if one already exists, the OHRP would be pleased to disseminate it.

Mr. McNulty, after complimenting Dr. Koski on his productive tenure with OHRP, expressed concern about the openness of accreditation organizations to working with or consulting with consumer groups. He referenced a recent conference in Indianapolis at which Dr. Koski spoke where apparently few members of the public were invited to participate. Mr. McNulty also commented that many IRB chairs appear to be confused about the Common Rule and need more case study examples to clarify how the regulations apply to particular situations. Dr. Koski thanked Mr. McNulty for this helpful suggestion and noted that, in this regard, NIH is not only developing guidance for working with human embryonic stem cells but also is disseminating a fact sheet of frequently asked questions and answers, with specific case examples.

ASSESSMENT OF DEPRESSION AND ANXIETY IN DEPRESSION TREATMENT TRIALS

Dr. Ellen Stover, Director of the Division of Mental Disorders, Behavioral Research and AIDS (DMDBA), briefed Council about recent activities by the Treatment Development Workgroup that is co-chaired by Drs. Dennis Charney and Wayne Fenton. A workshop on Assessment of Depression and Anxiety in Depression Treatment Trials, which was announced at the last Council meeting, was held in Washington, DC, on April 15-16, 2002. More than 120 persons attended—many more than the 35 originally anticipated. The attendees included academic researchers, representatives from about 50 pharmaceutical companies, persons in the test development industry, delegates from a variety of advocacy and professional organizations, and staff members from Federal agencies such as the FDA. Four members of this Council participated and/or spoke:
Drs. Scolnick, Nemeroff, and Knight-Richardson, and Mr. McNulty.

The workshop's major goal was to determine the best measures for assessing depressive symptoms in treatment trials with subjects who are adults, children, persons with comorbid somatic or anxiety disorders, or individuals undergoing psychotherapy. Five breakout groups were organized under designated chairpersons to address these target populations and the biological basis for core components. A corollary goal was to develop recommendations for a research agenda for identifying, refining, and/or creating better assessment tools to evaluate the efficacy and effectiveness of new depression treatments.

Highly qualified experts in 12 different aspects of depression and anxiety assessment addressed the workshop participants. The speakers were Drs. Charles Nemeroff, Dennis Charney,

John Rush, Janet Williams, Colleen McHorney, John March, Gary Sachs, K. Ranga Krishnan, Ellen Frank, Jonathan Davidson, William Potter, and Paul Andreasen.

A set of core questions developed by Drs. Stover and Fenton was posed to all breakout groups that focused on how best to utilize already available instruments for assessing depression and anxiety and how to improve or modify them during the interim while new measures of depression and anxiety are being developed or refined. As newly developed measures must be acceptable to the FDA, input from FDA's representatives was solicited at all points in the workshop discussions. Several questions focused on the particular endpoints that regulatory officials would accept as adequate current/interim evidence of efficacy in treatment trials for different target populations.

As a next step, the products from each breakout group will be presented and discussed at the new National Clinical Drug Evaluation Unit (NCDEU) meeting in June 2002. Special sessions will be devoted to this assessment effort as well as to the schizophrenia and cognition activities that are another focus of the Treatment Development Workgroup. An executive summary of the Washington, DC, workshop is being prepared for submission to two different scientific journals in the psychiatric and psychological domains. Finally, a Request for Applications (RFA) to solicit relevant research initiatives has been drafted.

CONCEPT CLEARANCE PRESENTATIONS

Coordinating Office in Support of the National NeuroAIDS Tissue Consortium (NNTC)

Dr. Stover explained the proposal to support the already existing National NeuroAIDS Tissue Consortium (NNTC) by developing a national NNTC Coordination Office under a 5-year contract mechanism. This independent office would support the Consortium's four existing brain-banking sites in Manhattan, Galveston, San Diego, and Los Angeles by serving as a central communication facility that will expand and maintain a secure tissue inventory database and assist researchers in formally requesting tissue and database materials.

Multiple Diagnoses in HIV-Infected Persons

Dr. Stover next described another AIDS-related concept as an initiative targeting HIV-infected persons with multiple comorbid diagnoses, particularly severe mental illness (SMI), substance abuse disorders, neurocognitive disorders, and other chronic health problems. Homeless persons of all ages are likely to have multiple diagnoses. Rates of HIV infection in persons with SMI are 13 to 76 times higher than those in the general population, depending upon the particular comorbidities found, and these other disorders may contribute to the likelihood of HIV infection.

The initiative will encourage attention to such comorbid conditions as the interaction of HIV infection and Alzheimer's disease; neurocognitive impairment in homeless individuals who are HIV-infected; separating out psychiatric from neurocognitive or neurological disorders that may have similar brain involvement, as distinguishing the behavioral aspects of depression from the

consequences of subcortical neurocognitive impairment is often extremely difficult; and the interaction of HAART (antiretroviral therapy) with other drug treatments for neurocognitive impairments and mental illness.

Approval of the Concepts

Without further discussion, a motion to approve both concepts was seconded and unanimously approved by the Council.

Research-Planning Grants for State Implementation of Evidence-Based Practices (EBPs)

Dr. Junius Gonzales, Chief of the Services Research and Clinical Epidemiology Branch of the Division of Services and Intervention Research (DSIR), described a proposed RFA that would stimulate state mental health agencies—through a P20 mechanism (exploratory grants)—to plan for and increase the implementation of evidence-based mental health services in local practice settings.

Within the last few years, clinical trials and other research studies have demonstrated the effectiveness of a number of mental health treatments. However, practitioners still have great difficulty transporting and translating these treatments into real-world settings. The science base for disseminating and implementing EBPs is vastly underdeveloped. The expectation is that this research-planning grant mechanism will encourage up to 10 commissioners of state mental health agencies to study the factors that affect implementation of EBPs in their mental health delivery systems. The long-term goal is not only to expand scientific knowledge regarding how to implement EBPs but also to establish mechanisms that ensure that new knowledge is rapidly incorporated into actual practice and that its impact is assessed.

Discussion

Dr. Wilson expressed strong support for this concept, noting that the issue was important throughout his tenure as President of the National Association of State Mental Health Program Directors and that the problem persists despite more recent cooperation among NIMH, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the state mental health authorities.

Dr. Nakamura reported that NIMH has been working with SAMHSA to build a stronger bridge between research and services. This proposed project is another attempt to strengthen those underpinnings and make certain that EBPs are implemented in the states where most services are actually delivered. This planning grant initiative is a critical component of translating research into practice and an important piece of the Institute's agenda.

Mr. English agreed that the proposed planning grants offer a perfect mechanism for NIMH and SAMHSA collaboration. A national EBPs project is already underway that was originally sponsored by the Robert Wood Johnson Foundation but is now supported by SAMHSA and others. The effort developed draft implementation tool kits for six different EBPs for people

with serious mental illness. The tool kits are about to be tested in an eight-state demonstration project that will consist of both individual and cross-state evaluations. By the time NIMH is ready to make awards under this concept, the field should already have a strong impetus to study EBP implementation activities.

Approval: After Dr. Nakamura called for a motion, which was made and seconded, this concept was unanimously approved.

FINAL REPORT: A STRATEGIC PLAN FOR DEPRESSION AND BIPOLAR DISORDER RESEARCH

Dr. Dennis Charney, Scientific Director of the Strategic Plan for Mood Disorders Research and Chief of the Mood and Anxiety Disorders Research Program in NIMH's Division of Intramural Research Programs, reviewed the development of the proposed strategic plan (available at http://www.nimh.nih.gov/strategic/stplan_mooddisorders.cfm) with the Council members for their discussion and approval. The impetus for the plan was based on three premises: (1) mood disorders are among the most serious and disabling of all medical conditions as recent studies by the World Health Organization and the Institute of Medicine (IOM) attest; (2) the Institute had gaps in its research portfolio on mood disorders, including making appropriate diagnoses, understanding pathophysiology, developing better treatments, and breaking down barriers to care; and (3) there have been breakthroughs in science that need to be applied to mood disorders. The task was to develop a strategic plan that would provide a unified direction for NIMH's research in mood disorders embracing the newest of scientific discoveries. The strategic planning process involved 200 participants, including 119 extramural scientists, 10 consumers and advocates, 63 NIMH staff, and 8 Council members.

To accomplish the task of reviewing the science and recommending how to spur scientific progress, NIMH convened nine scientific workgroups in January 2001 (see Appendix C for a listing of the workgroups and members). The workgroups convened in Pittsburgh in March 2001 to present and discuss preliminary reports; the workgroups finalized manuscripts, which they submitted in late 2001; the workgroup recommendations were consolidated and, through an iterative process extending from November 2001 to January 2002, developed and prioritized into implementation strategies. Drafts of the strategic plan continued to be refined until April 2002. Dr. Charney stated that the plan was being presented to Council at this time for its discussion and approval.

Professional staff at NIMH helped to develop the NIMH strategic plan, serving as workgroup members, consolidating recommendations from the different areas, developing objectives and implementation strategies, and providing additional scientific material as necessary to supplement the plan's development. An Executive Committee of senior NIMH staff (i.e., Drs. Charney, Fenton, Babich, Desimone, Foote, Norquist, Steinberg, and Stover) also reviewed the recommendations and implementation strategies as they were being developed, prioritized the objectives from the workgroups' reports, selected implementation strategies, and provided general oversight as the strategic plan was drafted. Dr. Charney gave special credit to Mr. Joseph Alper and Mr. Paul Sirovatka as the science writers of the plan.

The strategic plan contains three major sections reflecting different scientific perspectives—Basic and Clinical Neuroscience: Foundation for Discovery; Dimensions of Age and Disease; and Treatment, Services, and Prevention: Improving Outcomes. The plan also has an executive summary, an introduction, and appendices. The chapters are organized similarly, each focusing initially on the current status of the field, followed by a section on opportunities for progress, and concluding with recommendations for research priorities and an implementation plan.

Dr. Charney highlighted selected priorities in Section I of the plan. With respect to advancing genetic studies, one approach would be to identify and examine such heritable aspects of mood disorders as sleep parameters, circadian rhythms, hyperactivity, stress reactivity, or mood regulation. This approach corresponds to the development of animal models of circadian rhythm disturbances in mood disorders. Other objectives concerned the identification of measures of core symptoms of depression and mania that can be modeled in animals; the establishment of causality directions among factors that are known to be involved in mood disorders (e.g., neural, behavioral, experiential, genetic); and the enhancement of the Institute's capability to conduct postmortem studies by improving the brain-banking system so that changes in brain structure, circuitry, and gene expression related to mood disorders can be studied. Another set of priorities relates to opportunities to discover new drug and physiologic treatments and includes the establishment of long-term partnerships and collaborations among representatives of government, academia, and industry to accelerate drug discovery.

Section II of the plan focuses on identifying, treating, and preventing mood disorders across the life cycle and gaining a better understanding of the parameters of comorbidity. Questions regarding the differentiation of early-onset/adult-onset/late-onset depression need to be addressed. One example of a research priority needed to improve mental health in the elderly includes expanding the knowledge base of safe and effective treatments for late-life depression and associated suicide risk—an issue that has not had enough attention.

More knowledge is needed about depression as a major risk factor for cardiovascular disease, HIV/AIDS, cancer, diabetes, and stroke, and how, for example, the pathophysiology of these conditions overlaps to affect risk and prognosis. Also, more research should be conducted to improve the diagnostic validity of mood disorders in children and adolescents and to establish effective treatments for these target populations. Although the traditional approach has been to apply treatments that are effective for adults to children, this "top down" method may not be optimal, given the importance of developmental factors.

Dr. Charney displayed a timeline of mood disorders treatment strategies from the 1930s to the present, noting that each decade has seen advances in both medication/somatic and behavioral/psychosocial treatments for mood disorders. Tremendous progress has been realized since the 1930s when insulin-induced comas, convulsive therapy, and psychoanalysis were the only interventions for mood disorders. The 1950s and 1960s brought effective medications [the monoamine oxidase inhibitors (MAOIs) and the tricyclic antidepressants (TCAs)]; the 1970s witnessed the introduction of lithium treatment for bipolar disorder and cognitive behavioral therapy; and the 1980s saw the extension of treatment to many persons, largely resulting from

the safety of selective serotonin reuptake inhibitors and the consequent willingness of primary care providers to prescribe these medications as well as the availability of interpersonal therapy. By the 1990s, practitioners were using anticonvulsant drugs to treat mania and favored time-limited psychotherapies and psychoeducation. The new century has brought innovative uses of substance P, glutamate, N-methyl-D-aspartate (NMDA), and Web-based interactive interventions. The timeline also demonstrated how long translating research into widespread practice can take. For instance, cognitive behavioral therapy has been recognized as an effective treatment for depression for many years, but it is, nonetheless, not routinely available, partly because insufficient numbers of practitioners are trained in the necessary skills.

Section III of the plan outlines priorities for advancing research on treating and providing health care services for mood disorders. There is a basic need to determine how different interventions affect various phases of an illness in order to prevent symptom recurrence and relapse and to ascertain the long-term effects of interventions on patients' physiological and functional status.

Finally, prevention is a critical area for new research. Dr. Charney noted that the April 28 (2002) issue of *Science* contained several articles on the genetics and epidemiology of complex diseases that showed modifiable environmental risk factors (e.g., obesity, diet, and exercise) as they relate to heart disease and diabetes. At the moment, the modifiable environmental risks for developing mood disorders have not been quantified, but several are suspected. Some early life experiences, for example, appear to place individuals at greater risk for developing mood disorders. Identifying other modifiable environmental risks is an interesting approach to the prevention of mood disorders.

In concluding, Dr. Charney noted that he had highlighted only about one-third of the 52 objectives in the strategic plan. He noted that the plan would be available for comment on the NIMH Web site (see http://www.nimh.nih.gov/strategic/stplan_mooddisorders.cfm) until September 1, and invites readers' questions and comments on the plan, including their ideas for shaping the Institute's research agenda.

Discussion

Council members unanimously complimented Dr. Charney, staff, and the workgroups for developing a comprehensive strategic plan that will provide a useful template for future research.

Dr. Tsuang endorsed the plan's focus on prevention and applauded the focus on gene-environment interaction, reiterating the need to elucidate the interaction of susceptibility gene(s) with environmental factors.

Dr. Nemeroff proposed additions to the list of major gaps that need to be addressed: (1) research to identify predictors of response to various medications, e.g., lithium, valproic acid, or one antidepressant as opposed to another antidepressant. He noted that it is unclear whether studying brain images or single nucleotide polymorphisms (SNPs) might be helpful in predicting a response; (2) research on resilience and susceptibility genes to determine why some people do not become depressed while experiencing tremendous adversity or after early trauma.

Dr. Nemeroff noted that once there is a better understanding of how currently effective treatments work, progress may be made toward developing treatments with virtually no side effects.

Dr. Escobar commended the plan's approach in starting at a very basic neuroscience level and making the necessary research connections to ultimately arrive at the delivery of effective services. He suggested that 52 objectives might be too many and that presenting a hierarchy of goals might be more acceptable to legislators and other stakeholders. He stressed the importance of improving procedures for determining diagnoses in all subgroups.

Dr. Nestler asked whether a sufficient number of physician scientists and other types of researchers exist to conduct the proposed work. He said that although he realized the availability of qualified professionals was a consideration in drafting the document, he wondered whether the workgroups considered NIH initiatives to improve training and recruitment. Dr. Charney replied that every workgroup was concerned with improving the training infrastructure and that NIMH staff will be looking at ways to implement this objective.

Dr. Lieberman likened the mood disorders plan to the schizophrenia research initiative in the 1980s and hoped that it would have the same impact on the research field. He then asked for elaboration of a point Dr. Tsuang had raised about psychotic disorders, noting that unlike comorbidity in medical disorders, the symptomatic syndrome of depression occurs concurrently in psychosis, in dementia, and in anxiety disorders. Dr. Charney replied that this issue had been discussed in some detail across workgroups. The Development and Natural History Workgroup highlighted the finding that anxiety symptoms in children place them at great risk for developing serious mood disorders—like depression—later in life. It seems unlikely that one disorder early in life is anxiety related, while another disorder with later onset is unrelated. The issue has been handled in two ways: first, by defining comorbidity (e.g., having anxiety, psychosis, and mood symptoms at a given moment in time) in terms of biological processes and how to diagnose and treat the co-existing disorders and, second, as a developmental problem, in that symptom expression can differ as a function of the patient's stage of brain or psychosocial development. Again, the gene-environment interaction influences how genes are expressed over time.

Dr. Ritchie emphasized the importance of studying interactions at the neural and behavioral levels. Acknowledging the importance of the gene-environment interactions in the manifestation of illness, she posited that studying behavioral and neural interactions is at the heart of understanding depression. She commended the plan's balance in addressing research on pharmacological interventions and other psychological and behavioral treatments. She noted the value of interdisciplinary training in which students are exposed to both behavioral aspects of the disorders and the underlying neuroscience.

Dr. Durham voiced caution about embracing Web-based psychotherapy and asked others to comment on the utility of this intervention. Dr. Charney replied that the plan is quite circumspect about what can and cannot be done on the Web. However, at least two workgroups expressed interest in exploring Web-based therapies, with the appropriate safeguards, to provide patients with information about their illnesses, the research that has been conducted, and where

to get help with referrals. At a minimum, there seemed to be consensus that the Web could be used for psychoeducation. However, no specific recommendations were made to develop psychotherapy on the Web, although attempts have been made to conduct cognitive behavioral therapy on the Web, especially with teens who use this medium.

Dr. Scolnick observed that the plan offers an unparalleled opportunity for basic research findings to be translated into ongoing research on depression. For instance, a recent issue of *Biological Psychiatry* pointed out that patients who are at risk for depression have a slightly enlarged left amygdala—an extraordinary discovery because the amygdala is one of the better understood parts of the brain. The finding is potentially relevant to all who are studying development, neurogenesis, anatomy, and physiology. Additionally, the size of the amygdala could be another target for animal models.

Dr. Nemeroff commented that one of the great dichotomies in the field between animal and human research is that all animal models respond acutely to drugs, whereas human disease does not respond in this way; serious attention by researchers in animal genetics and human biology is needed to develop an animal model that more closely mimics the course of the human clinical response. Even if that can be achieved, there are still extremely difficult problems.
Dr. Nemeroff then emphasized the need to connect behavioral therapies with the emerging field of synaptic plasticity, based on what is known about learning in other situations; that is, any permanent behavioral changes must be associated with changes in the synapses and in synaptic strengths in different circuits.

Dr. Wilson reinforced Dr. Charney's remarks regarding disciplinary interactions that must be fostered and noted that interactions should be encouraged not only between neuroscience and clinical science but also between those entities and the service delivery system members as well. To recruit a broader spectrum of research subjects, NIMH investigators need to go to the areas where patients with more complicated and/or comorbid conditions are seeking treatment to try to engage clinicians in conducting specific research. This would help ensure that interventions have a generalizable impact.

Dr. Charney added that the lack of minority group participation in clinical trials is another reflection of health care disparities. Since few clinical trials are conducted at inner-city sites, study location, by itself, bypasses large population segments. He described a new initiative with the Howard University School of Medicine that is attempting to resolve this problem. The Division of Intramural Research Programs (IRP) is providing contractual funds for Howard to develop a research infrastructure and to collaborate with IRP staff in developing novel protocols that focus primarily on experimental therapeutics with patients who are evaluated and treated in the inner-city setting. Additional research will focus on the consequences of inner-city trauma.
Mr. McNulty commented on a front-page article in the current edition of *The Washington Post* on the interaction of placebo and other depression therapies that seemed misleading. He stressed the need to better inform the public on the role of placebos in drug trials. At several recent conferences, the pharmaceutical industry seemed to take the position that including placebo study arms is not helpful to understanding the value of tested treatments. Unless this issue is approached straightforwardly, Mr. McNulty said, NIMH would have an uphill battle to convince

the public that psychiatric medications and other treatments are ready for widespread distribution.

Dr. Charney agreed that the public's misconceptions concerning placebos are enormous. This was demonstrated to him earlier the same week when he appeared on a public radio program in response to the same article. More discussion is needed on the best research design, particularly in clinical trials, and a better explanation of placebos must be conveyed.

After Dr. Nakamura asked whether Council preferred to approve the strategic plan in its current form or send it back for another iteration, a motion was made for approval with staff incorporating Council's comments, and the motion was seconded. The Council unanimously voted approval.

IMPROVING MENTAL HEALTH CARE: NIMH SERVICES RESEARCH

Dr. Junius Gonzales, Chief of the Services Research and Clinical Epidemiology Branch (SRCEB), DSIR, reported on the status of services research at NIMH—research directed at improving mental health care for those who suffer from mental illnesses and their loved ones. After introducing himself as a psychiatrist who was fortunate enough to study under such luminaries in health services research as Dr. John Eisenberg and who personally experienced a lack of health insurance as a member of an immigrant laborer family, Dr. Gonzales set the stage for reporting current progress by recalling the history of health and mental health services research.

The services research community initially focused on the organization and financing of services. An historically important Fort Bragg study in the early 1990s (see, for example, Bickman, L.J. The evaluation of a children's mental health managed care demonstration. *Ment Health Adm* 23(1):7-15, 1996) sought to intervene at the system level by providing a continuum of integrated care for children and adolescents. This $80 million investment by NIMH, CHAMPUS (Civilian Health and Medical Program of the Uniformed Services) and other funders yielded both promising and disappointing results. On the positive side, the project increased client satisfaction and access to services and decreased dropout rates. However, the system-level interventions did not improve children's outcomes. Current mental health services research is trying to better understand how to impact the delivery of services. We face significant problems (e.g., a patient with major depression who goes to a psychiatrist in Washington, DC, to a psychologist in Northern Virginia, or to a social worker in Maryland, may not receive the same treatment or have the same outcomes after a year).

Health services research is a relatively new multidisciplinary area that was created less than 30 years ago with the establishment of a formal center within DHHS that eventually became the Agency for Healthcare Policy and Research (AHCPR) and was renamed the Agency for Healthcare Research and Quality (AHRQ) in 1999. In 2002, the Association of Health Services Research provided a new definition for health services research: "… the multidisciplinary field of scientific investigation that studies how *social factors*, financing systems, organizational

structures and processes, health technologies and *personal behaviors* affect access to health care, the quality and cost of health care and, ultimately, our health and well-being. Its research domains are *individuals, families,* organizations, institutions, *communities* and populations" (italics added by Dr. Gonzales for emphasis). Fortuitously, NIMH has been focusing on those emphasized factors for several years with the expectation that research in this field can meld scientific rigor with more immediate applicability.

A major contribution to this field that set the NIMH services research agenda was the 1999 Council report, *Bridging Science and Services* (see http://www.nimh.nih.gov/research/bridge.htm. That report concluded that NIMH research must be useful and practical for people with mental illnesses, clinicians, purchasers, and policymakers. Additionally, the report indicated that NIMH research should consider the domains of efficacy, effectiveness, practice, and service systems research in order to foster integration across fields and to expedite implementation.

The services research program at NIMH is broad, covering topics including population-specific initiatives, such as services for children and adolescents; the organization, delivery, and financing of mental health services in specialty mental health, general health, and other healthcare delivery settings; interventions to improve the quality and outcomes of treatment and rehabilitation services; research in rural settings; and dissemination and implementation research. Services research also offers promising opportunities to address some of the limitations of traditional randomized trials, such as studying "real-world" situations with high external validity and generalizability.

NIMH services research is housed in two divisions:

- In DSIR, the SRCEB has a research portfolio of more than 200 grants and has witnessed a 45 percent increase in services research applications between fiscal years 2001-2002, all without set-aside funding or RFAs. The SRCEB has ongoing programs in a variety of research areas, such as primary care, quality of care and outcomes, financing and managed care, systems research, sociocultural factors, research methods, and disablement and functioning. The SRCEB also sponsors many cross-training and cross-program activities.

- In DMDBA, excellent research programs on adherence, stigma, and health behavior are supported in several programs/branches and in the Center for Mental Health Research on AIDS.

NIMH is committed to setting new standards for rigor and relevance in services research as reflected in recent funding announcements. Notable among these are the following (see http://www.nimh.nih.gov/srceb/funding.cfm#mechs):

- The Interventions and Practice Research Infrastructure Development Program, using an R24 (resource-related research projects) mechanism, focuses on increasing the capacity to conduct research in real-world settings. As an example, this initiative might provide basic

staff and computer support for a family practice clinic in Anacostia that lacked these resources to enable the clinic to collect and interpret data.

- Several Program Announcements (PAs) in 2001 merged previous solicitations for research centers into more uniform and timely efforts to foster seamlessness and reflect the recommendations of the *Bridging* report to integrate science with communities, develop networks, provide core research methods, and promote innovation.

- The Time-Sensitive Opportunities PA also was developed in response to a recommendation in the *Bridging* report to encourage research that takes advantage of "now or never" opportunities. Since the real world does not necessarily operate on the same schedule as the NIH grant cycle, the review of some grant submissions must be expedited if opportunities to study changes in delivery systems, for example, are not to be lost.

- The R21 (exploratory/developmental grants) mechanism fosters emerging new areas of research.

- The concept for a new RFA that offers planning grants for state implementation of evidence-based practices was approved earlier in the day at this meeting.

The SRCEB is also trying to create new research approaches through conferences and workshops (see http://www.nimh.nih.gov/srceb/confs.cfm). A mental health services research conference entitled "Evidence in Mental Health Services Research: What Types, How Much, and Then What?" was held in April and had a record attendance of nearly 400 people. This was at least partially attributed to the excellent plenary speakers from fields outside of mental health. In addition, a number of workshops have addressed such issues as homelessness and child services implementation issues. An upcoming meeting will focus on pharmacoeconomics; the readily available funding offered by the private sector and industry for this type of work offers significant challenges.

Another approach to stimulating new research takes advantage of partnerships within the Federal Government and with other entities such as foundations or states. As an example, the Centers for Medicare and Medicaid Services (CMS), formerly the Health Care Financing Administration, sponsors a quality-improvement program using peer-review organizations. Last year, CMS funded two mental health grants that focus on important and vulnerable populations; one grant focused on improved depression screening and care for people who have had heart attacks. Other examples of new grants in the health services portfolio include:

- Creating a collaborative field research organization for traumatized children as part of an infrastructure development effort that partners a family services agency in New York City with 16 clinical sites and an academic institution to improve care and study seminal research questions.

- Helping homeless men transition from hospital to community—a research grant that carries a documented commitment by the state to continue and reimburse the effort if it is found to work.

- Screening more than 10,000 workers for six large employers and enrolling those found to be depressed in a number of treatment interventions.

- Improving the likelihood that Hispanic patients will continue in antidepressant therapy.

- Examining practice patterns for children with autism under one of two new services research grants in the autism portfolio that was funded in the last review cycle.

- Fostering collaboration between mental health and criminal justice staff for minor offenders with severe mental illness through a pending small business innovation research contract.

A number of opportunities and challenges face mental health services research. NIMH is endeavoring to open the field to innovation by recruiting researchers from relevant academic disciplines not traditionally associated with mental health (e.g., industrial engineering, management, and marketing sciences). Increased efforts are being made in the area of diffusion research to understand how new treatments can be incorporated into real-world practices and remain accessible to those who can benefit. Other cutting-edge research foci are the new NIMH aging consortium, disablement and functioning, criminal justice, community-based participatory research, and, as previously mentioned, pharmacoeconomics.

An article in the April 2002 issue of *The Journal of the American Medical Association* by Senator William Frist, M.D., addressed Federal funding for biomedical research. Senator Frist noted the need for continued improvements in the Nation's scientific framework and in the ability to translate research findings into practice, points that resonate with the NIMH approach. He asserted that the research process is not simply linear; phases must be conceptualized as an iterative process, since future phases are informed by, but can also improve, the design of earlier phases. Additionally, scientific knowledge can only be assimilated into practice through a series of process changes and the formation of numerous complex partnerships. NIMH's research program is designed to address these important issues.

Discussion

In thanking Dr. Gonzales, Dr. Nakamura explained that he had requested this presentation to underscore the Institute's commitment to services research and to enlist the support of Council members, as well as constituency groups and other members of the public attending this meeting, in continuing to build a robust program of research in this area. NIMH is also reaching out to other relevant agencies within the Federal Government and to the states to make them aware of mental health services research activities.

Dr. Lieberman complimented Dr. Gonzales for his thorough and informative presentation, particularly praising his obvious passion for the work and his multifaceted skills that serve the Institute so well, and Dr. Durham added her appreciation of Dr. Gonzales's leadership in this field that is so important for providers on the front lines in healthcare. The time is ripe, she stated, for healthcare delivery systems to implement evidence-based practices since providers are both interested and committed. Concomitantly, sophisticated clinical information systems are being developed that will be extremely useful tools for researchers. However, new legislation, the Health Insurance Portability and Accountability Act (HIPPA), is challenging privacy and confidentiality protections. The American public wants health information to be treated carefully and respectfully, and citizens have a right to say how that information should be used. However, because civil and criminal penalties will accrue under HIPPA to persons who handle health data inappropriately or make errors (not with a felonious intent), many healthcare organizations see a large risk in handing such data over to and partnering with researchers.

Nonetheless, Dr. Durham continued, other groups such as the State Mental Health Program Directors and health maintenance organization research networks would like to partner with NIMH to take advantage of the newly developing databases. The relationships between researchers and providers who have access to health-related data must be developed carefully as meaningful and trustworthy associations. This is a serious matter both for healthcare providers who want to see these data used effectively to contribute to the evidence base and for academics who want to conduct epidemiological studies and health services research.

Dr. Wilson reiterated the importance of NIMH support for mental health services research at this juncture when the Institute is expected to assume some of the services research activities previously assigned to SAMHSA. Parts of the mental health community applaud the application of more scientific rigor to the field, but NIMH also needs to adequately support innovative services research to truly advance the field. Dr. Gonzales replied that he was aware of the anxiety associated with the proposed fate of some SAMSHA programs, particularly a significant reduction in the Center for Mental Health Services' (CMHS) budget for this type of research. However, NIMH has not been transferred the budget authority or appropriation that is being reduced in CMHS. Despite this, the overall budget for services research within NIMH will approach $200 million.

Following up on the issue of changes in SAMHSA's mission and direction, Mr. English reported that CMHS has conducted only one generation of services research consisting of 12 multi-site studies that have been primarily concerned with understanding the interaction of multiple interventions for the same patient who has, along with family members, multiple psychiatric and medical disorders as well as related problems in living situations and clinical environments that substantially increase the risk for receiving minimal quality care. He stressed the importance of addressing a large number of environmental factors that potentially impact on patient outcomes in services research pertaining to multi-modal treatment in multiple-problem situations.
Mr. English said that CMHS has been concerned with these issues for the past 5 years and that, hopefully, NIMH will consider them relevant to its own portfolio and continue to synthesize the results of reliable efficacy research into a pattern of service delivery that makes sense organizationally, structurally, and financially.

Dr. Tsuang echoed this assessment, recalling that when the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) separated into SAMHSA, NIMH, NIDA, and NIAAA, SAMHSA retained a research component. The three Institutes under NIH also continue to support a services research component. It would seem to be an opportune time for NIMH and SAMHSA to collaborate on services research for the benefit of both entities. Dr. Nakamura reported that this process has already begun with meetings among staff from SAMHSA, NIMH, and CMHS to identify areas of common interest and potentially effective collaboration. Dr. Gonzales added that one of the grant applications that Council had approved the previous day was the first submission under the Time-Sensitive Opportunities Mechanism that he had previously described. The proposed project, which is a concrete example of services research with a complicated, multi-problem population, would build on a SAMHSA homelessness effort to study children in homeless families.

Voicing his appreciation of Dr. Gonzales's presentation, Mr. McNulty suggested that advocacy groups would likely be interested in the information conveyed about services research. He added that these groups are not always aware of the Institute's services programs and that he acquired much new knowledge about them today. Dr. Gonzales promised to follow-up on the suggestion and also noted that much of the information is available on the SRCEB's Web site (http://www.nimh.nih.gov/srceb/index.cfm).

In conclusion, Dr. Nakamura mentioned that NIMH, NIAAA, and NIDA are planning a technical assistance workshop for SAMHSA grantees whose funding is impacted by the proposed changes at SAMHSA about accessing other funding possibilities within NIH.

UPDATE ON THE CLINICAL TRIALS WORKGROUP

Dr. Jeffrey Lieberman, Professor and Vice Chairman of the Department of Psychiatry at the University of North Carolina, Chapel Hill, briefed Council on its newest Clinical Trials Workgroup. He reminded the audience that the workgroup was formed following NIMH's unprecedented support for large-scale, long-term contracted clinical trials in childhood depression, treatment-resistant depression, bipolar disorder, schizophrenia, and Alzheimer's disease, as well as the Institute's ongoing commitment to the support of clinical trials through a variety of grant mechanisms. Dr. Lieberman noted that the Institute sought advice in defining priority areas for funding, while ensuring that its portfolio adequately supports targeted research areas and utilizes a balanced range of funding mechanisms.

The workgroup's activities will include the following:

- Assessing the Institute's treatment research portfolio, particularly research supported in DSIR.

- Offering recommendations on whether the portfolio adequately addresses areas of greatest public health importance and takes advantage of the newest developments in treatment and service delivery methodology.

- Assessing funded studies' progress in meeting enrollment targets, adhering to approved schedules, and fulfilling Institute standards and expectations regarding efficiency and content.

- Identifying any deficiencies or gaps in treatment research where the field might be stimulated to develop new research projects.

- Identifying options to support treatment research evaluation.

Council membership in the workgroup includes Dr. Lieberman, who serves as chairperson, Drs. Escobar, Knight-Richardson, and Nemeroff, and Mr. McNulty. Experts from the extramural research community who represent key disciplines for evaluating treatment research have accepted invitations to join the workgroup, including Drs. Steven Hollon, Dilip Jeste, Helena Kraemer, M. Katherine Shear, and Karen Wagner. Planning is underway for the first meeting of this workgroup, and a report of the workgroup's deliberations will be provided at the Council's meeting in September.

Discussion

In response to a query from Dr. Nestler about the specific types of feedback and oversight the workgroup is expected to provide, Dr. Lieberman said that the first step will be to examine the Institute's current portfolio of treatment interventions research to ascertain whether it is broadly distributed across the relevant disease areas and different age groups and focused on optimal treatment methodologies or intervention strategies used in clinical psychiatry. If that is not the case, then the workgroup will identify areas of disproportionate emphasis or deficiency.

The next step, Dr. Lieberman continued, will be to examine if there is some disproportionate concentration of treatment intervention grants funded through some mechanisms or if there is a balance among the mechanisms. For example, DSIR and the other parts of the Institute have been concerned for a long time about the dearth of investigator-initiated applications that target certain diseases such as bipolar disorder. If all of the research in bipolar disorder is funded through contracts or cooperative agreements, there is probably some reason why investigators have not come forward spontaneously. By contrast, if many of the R01 applications in this area are not being funded because monies are being utilized to support studies via other mechanisms, some redirection may be needed.

Dr. Nestler observed that the process will require important interactions between the workgroup and NIMH program staff with respect to informing the extramural community about research areas in which investigators would and would not be encouraged to submit grants, based on current representation in the portfolio and emerging needs. Dr. Nakamura agreed with this description, adding that a major responsibility for the Institute will be to broadly disseminate clear messages about research gaps and opportunities to the research community, along with targeting funding to support new applications.

Dr. Leiberman had one important caveat: The particular number of funded grants in a specified portfolio area does not necessarily equate with adequate coverage unless the individual studies have met enrollment targets, have been completed on schedule, and have delivered the expected results.

Mr. McNulty concluded that the workgroup tasks are consistent with recommendations outlined in Dr. Charney's presentation of the strategic plan.

PUBLIC COMMENT

Dr. Darrel Regier, representing the American Psychiatric Association (APA), opened the public comment period by commending the approach taken in the strategic plan as presented by Dr. Charney. Dr. Regier said that the approach was useful for helping the APA conceptualize revisions of the DSM and consider how all aspects of research—from preclinical animal models through services research—should be applied to a given disorder. The APA will publish a series of white papers this summer on a range of diagnostic issues. Many Council members and NIMH staff have been actively involved in drafting these papers. Over the next 5 years, strategic plans will be developed that focus on some of the psychotic, anxiety, child and adolescent, and addictive disorders. These will examine how research can inform the understanding of different ways of categorizing disorders and the development of diagnostic criteria. Dr. Regier noted that the APA is grateful to NIMH for facilitating much of the work toward improving diagnoses, including the problems related to mixing phenotypes in the diagnosis of major depression. One possible option is to develop transient criteria as research progresses in specified areas and while more comprehensive diagnostic categories are explored.

Dr. Jerry Weyrauch from the Suicide Prevention Advocacy Network, USA, said the presentations helped him understand that his organization needs to be more involved with services research. Although a national strategy for suicide prevention has been promulgated, there are no scientifically proven interventions—only best practices that are sporadically evaluated. Currently, almost all of the 50 states fund suicide prevention efforts, but they are not sure how they should spend allocated funds, which range from $6 million in Minnesota to $250,000 in Georgia. Actually, Georgia plans to spend $30,000 to design an implementation and evaluation trial of a Gatekeeper Training Program that was identified as a key component in the national strategy but has not been thoroughly tested. More collaborations between public and private agencies are urgently needed to alleviate the tragic problem of suicide.

Ms. Monica Latham from the American Public Health Association (APHA) reported her enthusiasm for Dr. Charney's collaborative activities with Howard University to address health disparities, since this is a priority area for APHA as well. She also commended NIMH's services research projects that offer direct mental health services, adding that confidentiality can easily be protected in field studies by assigning patients random numbers instead of using actual names. Maryland has used this system successfully in reporting data to the Centers for Disease Control and Prevention and in collaborating with state and Federal projects.

Dr. Joan Levy Zlotnik, Executive Director of the Institute for the Advancement of Social Work Research, acknowledged NIMH's major contribution to the development and strengthening of social work research over the past decade. She stressed that social workers are the major deliverers of mental health services in this country, both as direct providers and as administrators. In fact, social workers are often the frontline caretakers who administer treatments to families and clients with multiple comorbid disorders that are too complex to be included in randomized clinical trials. Lack of community participation and organizational barriers to dissemination and diffusion of evidence-based practices are important concerns for social workers serving high-risk populations. Notably, too, both NIDA and the National Cancer Institute are emulating some of the models initiated by NIMH for strengthening their portfolios of social work research. Finally, Ms. Zlotnik expressed a desire to have the social work profession and social work researchers participate in advisory councils, workgroups, or other entities that focus on germane issues.

Ms. Patricia Watson, Deputy Director of Education at the National Center for Post-Traumatic Stress Disorder, asked the speakers on the Council agenda whether the mental health effects and mental health interventions following terrorism were being considered by the various workgroups. Dr. Ritchie responded that numerous efforts are underway in healthcare systems with large databases to develop some type of early-alert surveillance system. She presumed that other governmental agencies also are developing sophisticated systems for monitoring unusual findings following terrorist attacks or disasters and establishing a quick response capability. Dr. Gonzales added that, as described at the last Council meeting, the Institute supports the Rapid Assessment of Post-Impact Disaster (RAPID) grant program (see http://www.nimh.nih.gov/events/prrapidgrants.cfm), and staff has been working with several investigators who expect to apply for research grants relating specifically to training primary care providers.

Ms. Beth Kaplanek, representing Children and Adults with Attention-Deficit/Hyperactivity Disorder, reported that recent studies have found some gender-related factors that help explain the delayed identification of ADHD in girls and women. Because the DSM-IV does not provide adequate criteria for identifying females with this disorder, additional tools are necessary. Some structured self-reports might be helpful. Ms. Kaplanek also underscored the key role that parents play in advocating for their children who have mental health problems; parental empowerment can be crucial to their improved care and outcomes.

Mr. Paul Seifert, from the International Association of Psychosocial Rehabilitation Services, expressed concerns about implementing evidence-based practices that are derived from research. He noted that the majority of persons with anxiety or mood disorders have many other concurrent problems that cannot be handled in isolation. Further, much of services research and many evidence-based practices such as the Program for Assertive Community Treatment (referred to as PACT) and cognitive behavioral therapy date from the 1970s. The field has already advanced beyond these treatment approaches with peer-to-peer support programs and Web-based therapy. Unfortunately, current practices are not the focus of research.

Dr. Gary Kennedy, President of the American Association of Geriatric Psychiatry (AAGP), commended the strategic plan's goal to foster research on late-onset depression in the elderly and its emphasis on comorbidity, which appears to be the rule, not the exception, when working with older adults. The plans to recruit research participants with multiple problems, not just mental illnesses or cultural problems, are critical for older persons. With respect to training practitioners to become scientists, AAGP is advocating that clinicians, particularly those who specialize in geriatrics, be required to take additional training beyond the clinical requirements in order to acquire research skills.

Ms. Marjorie Kitzes, Vice President, Child and Adolescent Bipolar Foundation (CABF), noted that CABF, a parent-led advocacy and support organization for children with early-onset bipolar disorder, operates a virtual community center at http://www.bpkids.org/ that receives over 3,000 hits each day from parents, families, and providers all over the world who use the site to get information, support from other families, and referrals to appropriate treatment. The site does not provide therapy but does solicit many professionals to join and be listed as referral resources. With respect to improving health services research, Ms. Kitzes continued, there is a critical need to train persons as case workers who can provide a multi-pronged treatment approach—that blends educational, social, and therapeutic services—for children and adolescents with early-onset bipolar disorder who have needs that are different from those of adults.

As a final suggestion, Dr. Ritchie asked for a report at the next Council meeting on the workshop that Drs. Fenton, Tuma, and Dolan-Sewell are planning regarding benefits for and risks to subjects who participate in post-disaster or post-terrorist attack research efforts.

Adjournment

Whereupon, the 200th meeting of the NAMHC adjourned at 12:30 p.m. on May 10, 2002.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

_____

Richard K. Nakamura, Ph.D., Chairperson